3-methylcrotonyl-CoA carboxylase deficiency

Description

3-methylcrotonyl-CoA carboxylase deficiency (also known as 3-MCC deficiency) is an inherited disorder in which the body is unable to process certain proteins properly. People with this disorder have a shortage of an enzyme that helps break down proteins containing a particular building block (amino acid) called leucine.

Infants with 3-MCC deficiency appear normal at birth but usually develop signs and symptoms in infancy or early childhood. The characteristic features of this condition, which can range from mild to life-threatening, include feeding difficulties, recurrent episodes of vomiting and diarrhea, excessive tiredness (lethargy), and weak muscle tone (hypotonia). If untreated, this disorder can lead to delayed development, seizures, and coma. Many of these complications can be prevented with early detection and lifelong management with a low-protein diet and appropriate supplements. Some people with gene mutations that cause 3-MCC deficiency never experience any signs or symptoms of the condition.

The characteristic features of 3-MCC deficiency are similar to those of Reye syndrome, a severe disorder that develops in children while they appear to be recovering from viral infections such as chicken pox or flu. Most cases of Reye syndrome are associated with the use of aspirin during these viral infections.

Frequency

This condition is detected in an estimated 1 in 36,000 newborns worldwide.

Causes

Mutations in the *MCCC1* or *MCCC2* gene can cause 3-MCC deficiency. These two genes provide instructions for making different parts (subunits) of an enzyme called 3-methylcrotonyl-coenzyme A carboxylase (3-MCC). This enzyme plays a critical role in breaking down proteins obtained from the diet. Specifically, 3-MCC is responsible for the fourth step in processing leucine, an amino acid that is part of many proteins.

Mutations in the *MCCC1* or *MCCC2* gene reduce or eliminate the activity of 3-MCC, preventing the body from processing leucine properly. As a result, toxic byproducts of leucine processing build up to harmful levels, which can damage the brain. This damage underlies the signs and symptoms of 3-MCC deficiency.

Learn more about the genes associated with 3-methylcrotonyl-CoA carboxylase deficiency

- MCCC1
- MCCC2

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- 3-MCC
- 3-MCC deficiency
- 3-methylcrotonyl-coenzyme A carboxylase deficiency
- 3-methylcrotonylglycinuria
- 3MCC
- BMCC deficiency
- Deficiency of methylcrotonoyl-CoA carboxylase
- MCC deficiency
- Methylcrotonyl-CoA carboxylase deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: 3 Methylcrotonyl-CoA carboxylase 1 deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/CN028786/)
- Genetic Testing Registry: 3-MCC Deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268600/)
- Genetic Testing Registry: 3-methylcrotonyl CoA carboxylase 2 deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1859499/)

Genetic and Rare Diseases Information Center

- 3-methylcrotonyl-CoA carboxylase deficiency (https://rarediseases.info.nih.gov/diseases/10954/3-methylcrotonyl-coa-carboxylase-deficiency)

Patient Support and Advocacy Resources

- Disease InfoSearch (https://www.diseaseinfosearch.org/)
- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- 3-METHYLCROTONYL-CoA CARBOXYLASE 1 DEFICIENCY (https://omim.org/entry/210200)
- 3-METHYLCROTONYL-CoA CARBOXYLASE 2 DEFICIENCY (https://omim.org/entry/210210)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%283-methylcrotonyl-coa+carboxylase+deficiency%5BTIAB%5D%29+OR+%283-mcc%5BTIAB%5D%29+OR+%28mcc+deficiency%5BTIAB%5D%29+OR+%28methylcrotonyl-coa+carboxylase+deficiency%5BTIAB%5D%29+OR+%283-methylcrotonylglycinuria%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

References

- Arnold GL, Koeberl DD, Matern D, Barshop B, Braverman N, Burton B, CederbaumS, Fiegenbaum A, Garganta C, Gibson J, Goodman SI, Harding C, Kahler S, Kronn D, Longo N. A Delphi-based consensus clinical practice protocol for the diagnosisand management of 3-methylcrotonyl CoA carboxylase deficiency. Mol Genet Metab.2008 Apr;93(4):363-70. Epub 2007 Dec 21. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18155630)
- Baumgartner MR, Almashanu S, Suormala T, Obie C, Cole RN, Packman S, Baumgartner ER, Valle D. The molecular basis of human 3-methylcrotonyl-CoAcarboxylase deficiency. J Clin Invest. 2001 Feb;107(4):495-504. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11181649) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC199271/)
- Gallardo ME, Desviat LR, Rodríguez JM, Esparza-Gordillo J, Pérez-Cerdá C,Pérez B, Rodríguez-Pombo P, Criado O, Sanz R, Morton DH, Gibson KM, Le TP, Ribes A, de Córdoba SR, Ugarte M, Peñalva MA. The molecular basis of3-methylcrotonylglycinuria, a disorder of leucine catabolism. Am J Hum Genet.2001 Feb;68(2):334-46. Epub 2001 Jan 17. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11170888) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1235267/)
- Holzinger A, Röschinger W, Lagler F, Mayerhofer PU, Lichtner P, Kattenfeld T, Thuy LP, Nyhan WL, Koch HG, Muntau AC, Roscher AA. Cloning of the human MCCA and MCCB genes and mutations therein reveal the molecular cause of3-

methylcrotonyl-CoA: carboxylase deficiency. Hum Mol Genet. 2001 Jun1;10(12):1299-306. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11406611)

- Stadler SC, Polanetz R, Maier EM, Heidenreich SC, Niederer B, Mayerhofer PU, Lagler F, Koch HG, Santer R, Fletcher JM, Ranieri E, Das AM, Spiekerkötter U, Schwab KO, Pötzsch S, Marquardt I, Hennermann JB, Knerr I, Mercimek-Mahmutoglu S,Kohlschmidt N, Liebl B, Fingerhut R, Olgemöller B, Muntau AC, Roscher AA,Röschinger W. Newborn screening for 3-methylcrotonyl-CoA carboxylase deficiency: population heterogeneity of MCCA and MCCB mutations and impact on riskassessment. Hum Mutat. 2006 Aug;27(8):748-59. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16835865)

Page last updated on 18 August 2020

Page last reviewed: 1 October 2008